Title: Fructosamine; is the current interest in alternative glycaemic markers justified?

Running head: A role for fructosamine?

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Sir

Fructosamine; is the current interest in alternative glycaemic markers justified?

The interest in alternative glycaemic markers, such as fructosamine, has been rekindled due to increasing data on their ability to improve diagnosis [1] and predict onset and complications [2] of diabetes. Further clinical validation of these markers is called for [3] however the limitations must also be elucidated so, rather like HbA1c, the non-glycaemic physiological, pathological and analytical variables become well known.

Many of the variables that affect HbA1c appear to similarly affect fructosamine despite the different physiological compartments. The most commonly known non-glycaemic factor affecting fructosamine is albumin [3] although data on this is conflicting. We recently reported a multivariable univariate linear regression model of fructosamine (Table 3) [4] in which the effect of ethnicity (South Asian versus Caucasian), sex, age, presence of chronic kidney disease (CKD), vitamin B12, ferritin, folate, haemoglobin, mean cell volume (MCV), fasting glucose, HbA1c, albumin and C reactive protein (CRP) were examined [4]. The significant affect of albumin levels was confirmed as were the effects of ethnicity, age, presence of CKD (primarily CKD stage 3 versus CKD <3), vitamin B12, folate, albumin, CRP, fasting glucose levels, HbA1c and haemoglobin. Ferritin, MCV and sex were the only non-significant variables [4].

The large number of significant variables had not been anticipated, included due to their established effect on HbA1c, confirming our current poor grasp of fructosamine metabolism. Body mass index is also negatively associated with fructosamine in those without diabetes [5] and falls during pregnancy [6] further complicating its interpretation. Thyroid status may

affect fructosamine interpretation [3] however not necessarily independently of deranged glucose and protein metabolism [7].

We, therefore, read with interest the new data but would urge caution on the widespread adoption of fructosamine until the significance of non-glycaemic variables can be established in the clinical field. In particular HbA1c remains the biomarker of choice for monitoring glycaemic control in those with CKD [8], whereas fructosamine should be used with caution [4].

Yours sincerely

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